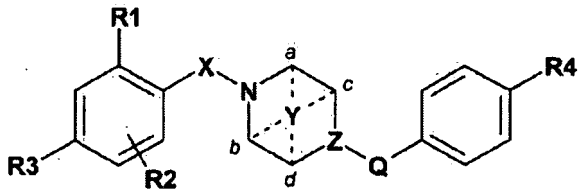
AMENDMENT TOTHE CLAIMS

1. (Currently Amended) A compound of formula I, or a pharmaceutically acceptable salt or ester thereof,



I

wherein

R1, R2 and R3 are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, ~~carbonyl,~~ amino, ~~sulfur,~~ cycloalkyl, heterocycloalkyl, aryl, heteroaryl; or substituted oxy, carbonyl, sulfur; or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle ~~for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl~~;

R4 is selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, ~~carbonyl,~~ amino, ~~sulfur,~~ cycloalkyl, heterocycloalkyl, aryl, heteroaryl or ~~a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl;~~ substituted oxy, carbonyl, sulfur;

X is –CH=CHCO-;

Y is ~~$-(CH_2)_n$ where n is 1-6,~~ $-CH_2OCH_2-$ ~~or $-CH_2NRCH_2-$~~ and is bonded to ~~two of the ring carbon atoms, bonding being to either the ring carbon atoms *a* and *b* or~~ the ring carbon atoms *c* and *d*; ~~wherein R is selected from the group consisting of H, optionally substituted: C_{1-7} alkyl, carbonyl, acyl, acetyl or sulfonyl;~~

Z is N or –CH-;

Q is $-CH_2-$, -NH- or -O-;

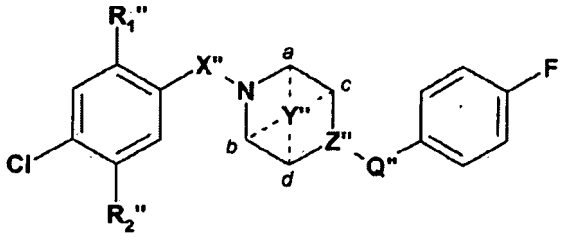
wherein when Z is N, Q is CH_2, and when Z is –CH-, Q is –NH- or –O-;

the optional substituents on ~~R1-R4~~ R1, R2, R3 and R4 are one or more, ~~e.g. 1-3~~ substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, aryl, heteroaryl, amino, or substituted oxy, sulfur, sulfinyl, sulfonyl;
wherein the optionally substituted substituents are optionally substituted once or more by~~, e.g. 1-6 substituents,~~ a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, ~~oxy,~~ hydroxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, amino, ~~sulfur,~~ cycloalkyl, heterocyloalkyl, aryl, heteroaryl; wherein oxy represents –O-; sulfur represents –S-, -S(O)- or $-S(O)_2-$ and carbonyl represents –C(O)-.

2. (Currently Amended) A compound of formula I as defined in claim 1 wherein R1 is an optionally substituted amino, amide, ~~guanidino,~~ sulfonyl, sulfonamide or heterocycloalkyl group, the optional substituents being selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, heterocycloalkyl, amino, or substituted oxy, sulfur, sulfinyl, sulfonyl;
wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, ~~oxy,~~ hydroxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, amino, ~~sulfur,~~ cycloalkyl, heterocyloalkyl, aryl.

3. (Previously Presented) A compound of formula I according to claim 1 wherein R2 is selected from the group consisting of methoxy, trifluoromethoxy, aryl, heteroaryl, C_{1-7} alkyl.

4. (Currently Amended) A compound according to claim 1, having the formula II, or a pharmaceutically acceptable salt or ester thereof:



II

wherein

R_1" and R_2" are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, ~~carbonyl,~~ amino, ~~sulfur,~~ cycloalkyl, heterocycloalkyl, aryl, heteroaryl or substituted oxy, carbonyl, sulfur; or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle ~~for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl;~~

X" is –CH=CHCO-;

Y" is ~~$-(CH_2)_n-$ where n is 1-6,~~ $-CH_2OCH_2-$ ~~or $-CH_2NRCH_2-$~~ and is bonded to ~~two of the ring carbon atoms, bonding being to either the ring carbon atoms *a* and *b* or~~ the ring carbon atoms *c* and *d*; ~~wherein R is selected from the group consisting of H, optionally substituted: C_{1-7} alkyl, carbonyl, acyl, acetyl or sulfonyl;~~

Z" is N or –CH-;

Q" is $-CH_2-$, -NH- or -O-;

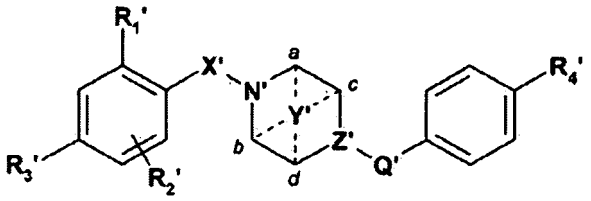
wherein when Z" is N, Q" is CH_2, and when Z" is –CH-, Q" is –NH- or –O-;

the optional substituents on R_1" and R_2" are one or more~~, e.g. 1-3~~ substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, aryl, heteroaryl, amino, or substituted oxy, sulfur, sulfinyl, sulfonyl;

wherein the optionally substituted substituents are optionally substituted once or more by~~, e.g. 1-6 substituents,~~ a substituent independently selected from the group consisting of

hydrogen, oxo, cyano, halo, nitro, ~~oxy,~~ hydroxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, amino, ~~sulfur,~~ cycloalkyl, heterocyloalkyl, aryl, heteroaryl.

5. (Currently Amended) A compound of formula Ia, or a pharmaceutically acceptable salt or ester thereof,



Ia

wherein

R_1', R_2' and R_3' are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, ~~carbonyl,~~ amino, ~~sulfur,~~ cycloalkyl, heterocycloalkyl, aryl, heteroaryl or substituted oxy, carbonyl, sulfur, or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle ~~for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl~~;

R_4' is selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, ~~carbonyl,~~ amino, ~~sulfur,~~ cycloalkyl, heterocycloalkyl, aryl, heteroaryl or substituted oxy, carbonyl, sulfur ~~a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl~~;

X' is $-OCH_2CO-$ or $-NHCH_2CO-$;

Y' ~~is $-(CH_2)_n-$ where n is 1-6,~~ $-CH_2OCH_2-$ ~~or $-CH_2NRCH_2-$~~ and is bonded to ~~two of the ring carbon atoms, bonding being to either the ring carbon atoms *a* and *b* or~~ the ring

carbon atoms *c* and *d*; ~~wherein R is selected from the group consisting of H, optionally substituted: C_{1-7} alkyl, carbonyl, acyl, acetyl or sulfonyl~~;

Z' is N;

Q' is $-CH_2-$;

the optional substituents on ~~R_1'-R_4'~~ R'_1, R'_2, R'_3, R'_4 being one or more substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted ~~oxy,~~ C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, aryl, heteroaryl, amino or substituted oxy, sulfur, sulfinyl, sulfonyl;
wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, ~~oxy,~~ hydroxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, amino, ~~sulfur,~~ cycloalkyl, heterocyloalkyl, aryl, heteroaryl; wherein oxy represents –O-; sulfur represents –S-, -S(O)- or $-S(O)_2-$ and carbonyl represents –C(O)-.

6. (Cancelled)

7. (Currently Amended) A compound of formula I, Ia, II, ~~Ib or IIb~~ as defined in claims 1, 4, 5 respectively, wherein the compound includes a radioisotope selected from the group of ^{11}C, ^{18}F, ^{75}Br, ^{76}Br, ^{80}Br, ^{123}I, ^{125}I, ^{128}I, ^{131}I, ^{13}N , ^{15}O.

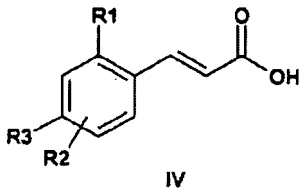
8-10 (Cancelled)

11. (Currently Amended) A method of ~~inhibiting chemokine receptors or of reducing inflammation in a mammal~~ treating a disease selected from the group consisting of rheumatoid arthritis, multiple sclerosis, Chronic Obstructive Pulmonary Disease, psoriasis, dermatitis and uveitis, in a human in need of such treatment which method comprises administering to said subject an effective amount of a compound according to claim 1.

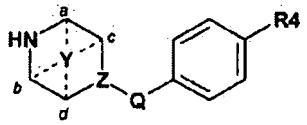
12-16 (Cancelled)

17. (Currently Amended) A process for the preparation of a compound of formula I, ~~II, Ia, Ib or IIb~~ according to claim 1 including the step of:

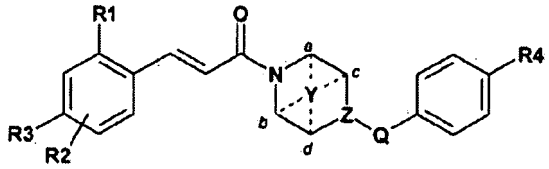
(a) ~~where the compound is of formula I or II, or of formula Ib or IIb wherein X is -CH=CHCO-,~~ condensing a compound of formula IV with a compound of formula V in the presence of a suitable amide coupling agent, ~~and, where Y is N, deprotection~~ to give the desired compound of formula I ~~(or corresponding compound of formula II, Ib or IIb)~~:



IV

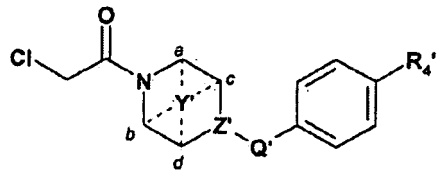


V

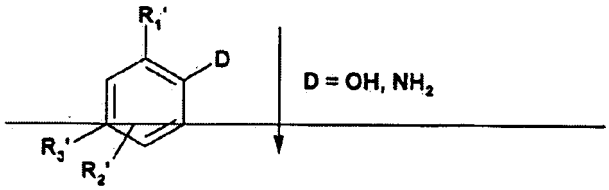


I

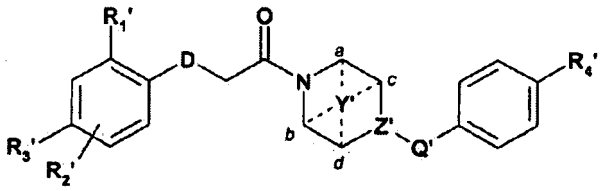
~~(b) where the compound is of formula Ia or II, or a compound of formula Ib or IIb wherein X is $-OCH_2CO-$, or $-NCH_2CO-$, reacting a compound of formula X with a compound of formula IX in the presence of a strong base in an inert organic solvent:~~



IX



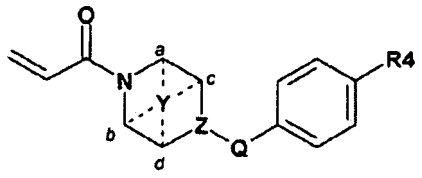
X



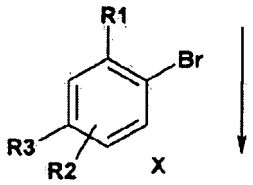
XI

or

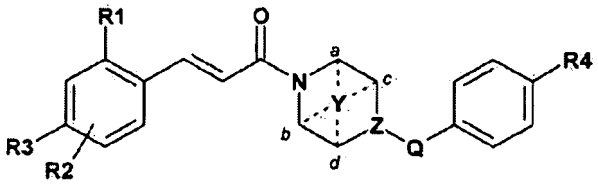
~~(c) where the compound is of formula I or II, or of formula Ib or IIb wherein X is CH=CHCO,~~ (b) reacting a compound of formula X with a compound of formula XII in the presence of a suitable reagent ~~such as a palladium catalyst~~ and a base to produce the desired compound of formula I:



XII



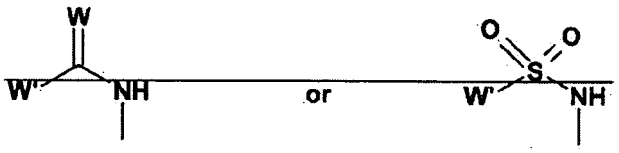
X



I

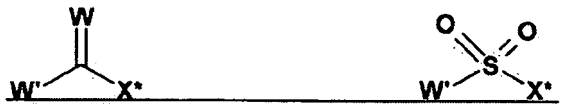
~~or~~

~~(d) where the compound is a compound wherein R1, R_1' or R_1" is denoted by a group of the following formula:~~



~~wherein W is O or a nitrogen carrying optional substituents and W' represents optional substituents,~~

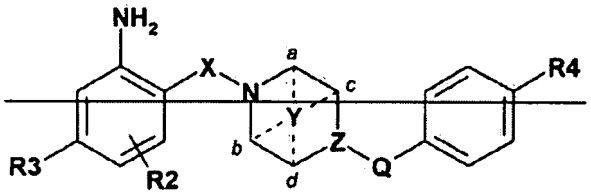
~~reacting a corresponding compound of formula XII or XIII:~~



XII XIII

~~wherein X* represents a leaving group, for example chloro,~~

~~with a compound of formula XV:~~



~~XV~~

~~to produce the desired compound~~

wherein the substituents of Formulae IV, V, X, XII are as defined in Formula (I) of claim 1 for the corresponding substituents.

18. (Original) A process according to claim 17, further including the step of temporarily protecting any interfering reactive groups and/or then isolating the resulting compound of the invention.

19. (New). The compound of claim 1 wherein R1, R2 and R3 are independently a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle; which substituent is butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl.

20. (New). The compound of claim 5 wherein R1', R2' and R3' are independently a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle; which substituent is butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl.